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Patrice Jacques Marie Pellerin

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EXAMINER

LEAVITT, MARIA GOMEZ

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/582,987	Applicant(s) PELLERIN ET AL.	
	Examiner MARIA LEAVITT	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02-24-2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 1-4,8,9 and 11-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-7,10 and 14-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 June 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06-15-2006</u> . | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

Applicants' response to the restriction requirements of 04-09-2009 has been entered.

Claim status. Claims 1-19 are currently pending. Claims 5, 6 and 11 have been amended and claims 14-19 have been added by Applicants' amendment filed on 02-24-2009. Applicants' election **with traverse** of Group IV, drawn to an isolated nucleic acid of SEQ ID No. 28 encoding the HXT3 hexose transporter, i.e., claims 5, 6, 7 (in part) 10, and new claims 14-19, in Applicants' response filed on 02-24-2009 is acknowledged.

Response to arguments

At page 6 of Applicants' Response filed on 02-24-2009, Applicants essentially argue that the restriction is improper because the claims of the elected invention are directed to isolated nucleic acids which encode for a HXT3 hexose transporter comprising one or more mutations compared with that of the wild type. In addition, claim 5 is a generic claim and the examination should include the nucleic acid molecules of SEQ ID NO: 28 and 29, as they both are species of the same generic claim 5. The above arguments have been fully considered but deemed unpersuasive.

As stated in the restriction requirements filed on 01-22-2009, Groups IV, elected by Applicants, drawn to an isolated nucleic acid of SEQ ID NO: 28, and Group V, drawn to an isolated nucleic acid of SEQ ID NO: 29, do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features. In the present claims, a polynucleotide of Group IV does not necessarily encode a polypeptide of Group V, for example. In addition, the MPEP §803.04 states, "normally ten sequences constitute a reasonable number for examination purposes." The waiver for up to 10

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nucleotide sequences is permissive and not a requirement. The waiver went into effect in 1996, well before the exponential growth of the nucleic acid and protein databases. Since the addition of these guidelines to the MPEP the biological sequence databases required to be searched for the examination of any biological sequence have grown tremendously (e.g. a 54-fold increase in the number of nucleic acid sequences in the GenBank data base and a 91-fold increase in the number of nucleotides between 1996 and February 2006), and thus the Technology Center no longer routinely examines and searches more than one independent biological sequence for any single application (a pre-OG notice <http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/sequence02212007.pdf>). The present restriction requirement conforms with this policy as it has required that the application be restricted to two polynucleotide sequence. Hence searching for more than one SEQ ID would be unduly burdensome to the examiner.

Additionally, no specific argument or evidence is presented by Applicant demonstrating that the species of SEQ ID NOs. 28 and 29 are not patentably distinct or obvious variant of each other. Indeed, Applicants assert at page 6 of Remarks, that SEQ ID No. 29 has the mutation of SEQ ID No. 28, and additional mutations according to Table 3B of the Specifications. Thus, each invention is mutually exclusive such that a search for the polynucleotide of SEQ ID No. 28 would not find the polynucleotide of SEQ ID No. 29. Thus the search for each invention is not coextensive, such that the search and examination of two inventions together would place an undue burden on the examiner. Moreover, the burden is due to the need to search different classes/subclasses or electronic resources, or employing different search queries, and/or the

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different inventions raising different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C.

112, first paragraph. Hence, restriction is proper.

However, upon the allowance of generic claim 5, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.14. If claims are added after the election, applicant must indicate which are readable upon the elected species.

MPEP 809.02(a)

Accordingly, claims 1-4 and 8, 9, 11-13 are withdrawn for further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

The examiner notes that MPEP 1893.03(d) states:

If an examiner (1) determines that the claims lack unity of invention and (2) requires election of a single invention, when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. Any nonelected product claim that requires all the limitations of an allowable product claim, and any nonelected process claim that requires all the limitations of an allowable process claim, should be rejoined. See MPEP § 821.04 and § 821.04(a). Any nonelected processes of making and/or using an allowable product should be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

The requirement is still deemed proper and is therefore made FINAL.

Note the examiner does not considerer necessary a supplemental restriction in response to the filing of new claims 14-19 on 02-24-2009. Also note that new claims 14-19 are examined to the extent that they read on the elected species: SEQ ID NO: 28.

Therefore, claims 5-7 10, (in part) and new claims 14-19 are currently under examination to which the following grounds of rejection are applicable.

Priority

The present application is a 35 U.S.C. 371 national stage filing of International Application No. PCT/EP2004/014577, filed December 20, 2004, which claims priority to prior-filed EP 03078992.9, filing date December 19, 2003. Filing on 06-15-2006 of a certified translated copy is acknowledged.

Objection Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claim 6 recites, “The nucleic acid according to claim 5, having a sequence according to SEQ ID NO: 28” . There is a not proper antecedent base for said nucleic acid sequence of SEQ D No. 28 in the specification as filed. Likewise claim 15 recites “the nucleic acid according to claim 14, which comprises the nucleotide sequence of SEQ ID NO: 28”. There is a not proper antecedent base for said nucleic acid sequence of SEQ D No. 28 in the specification as filed

Specification Objection

At page 7, line 15 and page 11, lines 14 and 24, of the as-filed specification, the use of the trademark Fermichamp® has been noted without capitalization. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which may affect their validity as trademarks.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 15-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language.

Claims 15-19 recite the term “derived”. The metes and bounds of this term are indefinite because “derived” can encompass multiple meanings from the origin of something to deducing something. Therefore, the intended mean of the term, “derived” is vague and indefinite. Recitation of term “obtained or isolated from” in place of derived would obviate the basis of this rejection. Appropriate correction is required.

For the purpose of a compact prosecution the claims have been interpreted as “an isolated nucleic acid encoding a mutated HXT3 hexose transporter with an improved capacity to transport carbohydrates wherein said encoded amino acid sequence is isolated from SEQ ID No. 26”.

Additionally, claim 19, at lines 5-6, recites “and Leu 471 Ile”. It is unclear whether they are two optional amino acids at position 471 of SEQ ID No. 26, or a Leu residue has been replaced with an Ile, alternatively, an Ile residue has been replaced with a Leu. As such, the metes and bounds of the claims cannot be determined.

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Claim Rejections - 35 USC § 112-First paragraph-Scope of Enablement

To the extent that claims 6 reads on a functional homolog of the nucleotide sequence of SEQ ID No. 28, the following rejection applies.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising the full length of SEQ ID No. 28 encoding the HXT3 hexose transporter, does not reasonably provide enablement for a functional homolog of SEQ ID No. 28 .

The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with this claim. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat.

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App. & Inter, 1986) and *In re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) Nature of invention. The invention recites an isolated sequence comprising SEQ ID No. 28 or a functional homolog encoding a functional the HXT3 hexose transporter. A “functional homolog of SEQ ID No. 28” as best understood, reads on a genus of isolated a nucleic acid sequences encoding for the HXT3 hexose transporter with an improved capacity to transport fructose in relation to the wild type hexose transporter of SEQ IS No. 26. This invention utilizes disciplines of recombinant technology as well as protein production. As well, assays for “functional” fragments” among the recombinant molecules are required to perform the invention.

2) Scope of the invention. The fragments can encode for any amino acid molecule with any number of deletions at the N-terminus or C-terminus. Therefore, claim 6 recites a broad collection of nucleic acid molecules that may not retain full or even partial activity.

3) Number of working examples and guidance. While the sequence of SEQ ID NO: 28 is taught in the specification, no examples of fragments of the HXT3 hexose transporter or what domains or regions are required for function of the HXT3 hexose transporter. Therefore, there is no indication of a structure-function relationship between the sequence of SEQ ID NO 28 and the HXT3 hexose transporter activity. Furthermore, the instant specification fails to demonstrate any examples or specific guidance for the identification or isolation of “functional fragments” of SEQ ID NO: 28, i.e. assays for the analysis of the HXT3 hexose transporter fragments that would meet the limitations of the claims. The specification as filed discloses localization of the 10 mutations in Hxt3-Fmp clustered in TM9 and an external loop between TM9 and TM10 (Fig.

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1) and functional analysis of the Fermichamp (e.g., an industrial *S. cerevisiae* wine strain) *HXT3* allele by expressing it in an *hxt1-7Δ* deletion strain unable to ferment hexoses. The guidance for the isolation and sequence analysis of the Fermichamp *HXT3* allele with mutations that modify its fructose kinetics is provided in the specification. However, no guidance is given for the isolation of “functional” homologs of the HXT3 hexose transporter.

4) State of the art. Recombinant technology for the generation of new protein fragments is highly developed. However, the ability to determine *a priori* whether a mutation will generate a functional fragment is not. The art must therefore be considered to be poorly developed. It is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo et al, 1994). The skilled artisan understands that one nucleotide change in a DNA molecule or one amino acid change in the polypeptide encoded by the DNA molecule could result in the loss of its biological activity as demonstrated in the generation of sickle-cell anemia wherein one specific amino acid mutation gave rise to the inherited disease (Biochemistry, John Wiley and Sons, 1990, p. 126-129). Rudinger (in Peptide Hormones, 1976) discloses that even for peptide hormones, which are much smaller than the instant peptide of SEQ ID No. 15, one cannot predict variant amino acid sequences for a biologically active polypeptide. Rather one must engage in “case to case painstaking experimental study” to determine active variants (see page 6). Even single-nucleotide polymorphism without affecting the amino acid sequence can affect folding of the protein and thus alter its function (Kimchi-Sarfaty et al., 2007, Science, pp. 525-528; p. 527, col. 3, last paragraph).

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5) Unpredictability of the art. Since there were no other examples of functional sets of polynucleotide variants encoding the HXT3 hexose transporter, it is not possible to even guess at the amino acid residues which are critical to its structure or function based on sequence conservation. Without knowing the structure-function relationship of SEQ ID NO:28, the ability to predict the effect of mutations on function is highly unpredictable.

6) Amount of Experimentation Required. The invention recites isolated functional fragments of the HXT3 hexose transporter. In view of the unpredictability of the art of predicting the functional nature of fragments of SEQ ID NO 28 encoding for the functional HXT3 hexose transporter deleted of any number of amino acids from the C-terminus and/or the N-terminus: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. Given the unpredictability of the art, the poorly developed state of the art with regard to predicting the structural/ functional characteristics of a protein from primary amino acid sequence alone, the lack of working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue, unpredictable experimentation to practice the claimed invention.

Claim Rejections - 35 USC § 102(b)

To the extent that claims 5, 7, 10, 14, and 16 read on an isolated nucleic acid encoding a mutated HXT3 hexose transporter with an improved capacity to transport carbohydrates as compared to a wild type hexose transporter encoded by SEQ ID No. 26, with at least a mutation selected from the group consisting of Gln 206, Leu 207, Met 208, Ile 209, Thr 210, Leu 211 and Gly 212, e.g., Gln 206, the following rejection applies.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 5, 7, 10, 14 and 16 are rejected under **35 U.S.C. §102(b)** as being anticipated by Liang et al., (1998, Molecular and Cellular Biology, pp. 926-935; of record) as evidenced by Ko et al., (1993, Molecular and Cellular Biology, pp. 638-648).

Liang et al., discloses isolated nucleic acid molecules encoding hexose transporter mutants able to restore glucose-dependent growth to yeast cells containing null alleles of all of the known functional glucose transporter genes upon introduction of the plasmid encoding said hexose transporter mutants (p. 926, col. 2, paragraph 2; p. 928, col. 1, paragraph 1). The HXT3 hexose transporter suppressor mutants alter sites that are highly conserved in *S. cerevisiae* at residues that lie within or immediately adjacent to putative membrane-spanning domains including the HXT3-206 mutant, wherein Gln²⁰⁶ → Lys or Arg at TM5 (p.928, col. 1, paragraph 2; p. 928, Table 1; p.930, Fig. 3). Note that the sequence of the wild type glucose hexose transporter gene taught by Liang et al., encodes a HXT3 (accession no. L07080) having 100% identity with the HXT3 of SEQ ID No. 26 of the instant invention as evidenced by the nucleotide and deduced amino acid sequence illustrated in Fig. 2, at page 641 of the Ko et al., publication.

Thus by teaching all the claims limitations, Liang et al., anticipate the instant invention.

Claim Rejections - 35 USC § 102(b)

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To the extent that claims 6 and 15 read on an isolated nucleic acid comprising the nucleotide of SEQ ID NO. 28, which is broadly interpreted as encompassing nucleic acids that comprise the full length of SEQ ID No. 28 with or without additional nucleotides at either or both sides, the following rejection applies.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6 and 15 are rejected under **35 U.S.C. §102(b)** as being anticipated by Contreras et al., (WO200264766-A2, Date of publication 22 Aug 2002; Score search results. Application 10582987 and Search Result 20090526_161013_us-10-582-987-28.rng.”).

Contreras et al., teaches a nucleotide sequence of ID ABQ76349 of 2211 nucleotides in length representing a synthetic CC Bax gene having 100% homology to the nucleotide sequence of instantly disclosed SEQ ID NO: 28 of 1704 nucleotides in length (See Result 4 on the attached search print out titled “Application 10582987 and Search Result 20090526_161013_us-10-582-987-28.rng.”).

Thus by teaching all the claims limitations, Contreras et al., anticipate the instant invention.

Claim Rejections - 35 USC § 103

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To the extent that claims 14 and 17-19 read on an isolated nucleic acid encoding a mutated HXT3 hexose transporter with an improved capacity to transport carbohydrates as compared to a wild type hexose transporter encoded by SEQ ID No. 26, with at least a mutation selected from the group Gln 206, Leu 207, Met 208, Ile 209, Thr 210, Leu 211 and Gly 212, e.g., Gln 206, and further comprising at least a mutation selected from the group consisting of Met 324, Leu 388, Ile 392, Glu 414, Gly 415, Ile 449 and Leu 471, the following rejection applies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14 and 17-19 are rejected under 35 USC 103 as being unpatentable over Liang et al., (1998, Molecular and Cellular Biology, pp. 926-935; of record), in view of Liang et al., as evidenced by Ko et al., (1993, Molecular and Cellular Biology, pp. 638-648).

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Liang et al., discloses isolated nucleic acid molecules encoding hexose transporter mutants able to restore glucose-dependent growth to yeast cells containing null alleles of all of the known functional glucose transporter genes upon introduction of the plasmid encoding said hexose transporter mutants (p. 926, col. 2, paragraph 2; p. 928, col. 1, paragraph 1). Note that the sequence of the wild type glucose hexose transporter gene taught by Liang et al., encodes a HXT3 (accession no. L07080) having 100% identity with the HXT3 of SEQ ID No. 26 of the instant invention, as evidenced by the nucleotide and deduced amino acid sequence illustrated in Fig. 2, at page 641 of Ko et al., publication. Additionally, the HXT3 suppressor mutants disclosed by Liang et al., alter sites that are highly conserved in *S. cerevisiae* at residues that lie within or immediately adjacent to putative membrane-spanning domains including the HXT3-206 mutant wherein Gln²⁰⁶ → Lys or Arg at TM5 (p.928, col. 1, paragraph 2; p. 928, Table 1; p.930, Fig. 3). Liang et al., teaches other 24 suppressor mutations located adjacent to TM1, TM2, TM4 through TM7, TM10 and TM12 which alter the structure of the putative TMs or the region in the first extracellular loop immediately adjacent to TM1 (p. 928, col. 1, paragraph 2; Table 1). Though Liang et al., does not explicitly teach at least amino acid mutations located at residues Met³²⁴, Leu³⁸⁸, Ile³⁹², Glu⁴¹⁴, Gly⁴¹⁵, Ile⁴⁴⁹ or Leu⁴⁷¹, Liang et al., clearly describes HXT3T mutants with mutations that lie within or immediately adjacent to putative membrane-spanning domains that are critical to mediate glucose transport, for example, mutations that lie within or immediately adjacent to TM7 and disrupt TM7, e.g., Ser³³⁰, Gln³³², Leu³³⁴ and Gly³³⁶ (reading on the instantly claimed Met 324 mutation), mutations clustered within TM10 and disrupting TM10 e.g., Ala⁴³⁸, Ala⁴⁴² (reading on instantly claimed Ile⁴⁴⁹) and others (See Fig 2 and Table 1 to map location of single amino acid mutations in the twelve-TM model of Hxt3).

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Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made, to generate HX3T mutants employing any combination of conserve residues in *S. cerevisiae* that lie within or immediately adjacent to putative membrane-spanning domains in an attempt to provide an isolated nucleic acid encoding a mutant HX3T with improved glucose transport. At the effective filing date of the present application, the predicted topology of the putative membrane-spanning domains in HXT3 was known in the art as evidenced by the Ho et al., publication. The manipulation of previously identified DNA fragments and cell transformation systems for the design of a novel nucleic acid encoding a mutant HXT3 is within the ordinary level of skill in the art of molecular biology. The mere combination of mutated residues in *S. cerevisiae* that lie within or immediately adjacent to putative membrane-spanning domains has no patentable significance unless a new and unexpected result is produced. Thus it would have been *prima facie* obvious to one skilled in the art to mutate known amino acid residues at locations that are critical for the transport of glucose with a reasonable expectation of success in an attempt to generate a genetically engineered yeast (e.g., *S. cerevisiae*) with enhanced glucose transport capacity, as a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. In turn, because the claimed isolated nucleic acid has the properties predicted by the prior art, it would have been obvious to make the claimed mutant HXT3.

Conclusion

Claims 5-7, 10 and 14-19 are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/Maria Leavitt/

Maria Leavitt, PhD
Examiner, Art Unit 1633